

FILE 'HOME' ENTERED AT 13:25:09 ON 28 NOV 2003

=> file agricola biosis caplus caba

=> s lectin and cry?

L1 2061 LECTIN AND CRY?

=> s lectin and cryi?

L2 21 LECTIN AND CRYI?

=> duplicate remove l2

L3 18 DUPLICATE REMOVE L2 (3 DUPLICATES REMOVED)

=> d ti 1-18

L3 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Altered glycosylation of 63- and 68-kilodalton microvillar proteins in *Heliothis virescens* correlates with reduced Cry1 toxin binding, decreased pore formation, and increased resistance to *Bacillus thuringiensis* Cry1 toxins

L3 ANSWER 2 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1

TI PCR detection of transgenic elements in feed raw material.

L3 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Linear transgene constructs lacking vector backbone sequences generate transgenic rice plants which accumulate higher levels of proteins conferring insect resistance

L3 ANSWER 4 OF 18 CABA COPYRIGHT 2003 CABI on STN

TI Detection of transgenic elements in feed materials by PCR method.

L3 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Novel primer pairs for detection of genetically engineered plant material in food

L3 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI PCR method for detecting recombinant DNAs from genetically modified crops and processed food

L3 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Expression of multiple insecticidal genes confers broad resistance against a range of different rice pests

L3 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Fusion proteins comprising *Bacillus thuringiensis* CryIA(b,c) toxins and ricin B chain fragments and their pesticidal activities

L3 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Method for producing transgenic plants resistant to glyphosate herbicides

L3 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Method for producing transgenic plants resistant to glyphosate herbicides

L3 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Method for producing transgenic plants resistant to glyphosate herbicides

L3 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Detection of genetically modified soybeans and maize by the polymerase chain reaction method

L3 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Partial purification and characterization of *Bacillus thuringiensis* CryIA toxin receptor A from *Heliothis virescens* and cloning of the corresponding cDNA

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Expression of two insect-resistant genes cryIA (b&c)/GNA in transgenic tobacco plants results in added protection against both cotton bollworm and aphids

L3 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Construction of plant expression vector harboring two insect-resistant genes and their expression in tobacco

L3 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI Factors affecting the binding of the *Bacillus thuringiensis* crystal protein, Cry1Ba, to *Wiseana cervinata* brush border membrane vesicles

L3 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

TI The receptor for *Bacillus thuringiensis* CryIA(c) delta-endotoxin in the brush border membrane of the lepidopteran *Manduca sexta* is aminopeptidase N

L3 ANSWER 18 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 2

TI N ACETYL GALACTOSAMINE IS PART OF THE RECEPTOR IN INSECT GUT EPITHELIA THAT
RECOGNIZES AN INSECTICIDAL PROTEIN FROM BACILLUS-THURINGIENSIS.

=> d bib abs 17 15 14 13 7

L3 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1994:238222 CAPLUS

DN 120:238222

TI The receptor for *Bacillus thuringiensis* CryIA(c) delta-endotoxin
in the brush border membrane of the lepidopteran *Manduca sexta* is
aminopeptidase N

AU Knight, Peter J. K.; Crickmore, Neil; Ellar, David J.

CS Dep. Biochem., Univ. Cambridge, Cambridge, CB2 1QW, UK

SO Molecular Microbiology (1994), 11(3), 429-36

CODEN: MOMIEE; ISSN: 0950-382X

DT Journal

LA English

AB A 120 kDa glycoprotein in the larval midgut membrane of the lepidopteran
Manduca sexta, previously identified as a putative receptor for *Bacillus*
thuringiensis CryIA(c) delta-endotoxin, has been purified by a
combination of protoxin affinity chromatog. and anion exchange chromatog.
In immunoblotting expts., the purified glycoprotein has the
characteristics predicted of the receptor: it binds CryIA(c) toxin in the
presence of GlcNAc but not GalNAc; it binds the lectin SBA; but
it does not bind CryIB toxin. N-terminal and internal amino
acid sequences obtained from the protein show a high degree of similarity
with the enzyme aminopeptidase N (EC 3.4.11.2). When assayed for
aminopeptidase activity, purified receptor preps. were enriched 5.3-fold
compared to *M. sexta* brush border membrane vesicles. The authors propose
that the receptor for CryIA(c) toxin in the brush border membrane of the
lepidopteran *M. sexta* is the metalloprotease aminopeptidase N.

L3 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:805078 CAPLUS

DN 133:1270

TI Construction of plant expression vector harboring two insect-resistant
genes and their expression in tobacco

AU Wang, Zhibin; Guo, Sandui

CS Lab. of Biochemistry and Molecular Biology, Biotechnology Research Center,
Chinese Academy of Agricultural Sciences, Beijing, 100081, Peop. Rep.
China

SO Gaojishu Tongxun (1999), 9(11), 001-006

CODEN: GTONE8; ISSN: 1002-0470

PB Gaojishu Tongxun Zazhishe

DT Journal

LA Chinese

AB A synthesized *Bacillus thuringiensis* insecticidal crystal protein gene
cryIA and synthesized GNA (the mannose specific lectin
from snowdrop (*Galanthus nivalis*)) were inserted into plasmid pBI121.1 to
obtain plant expression vector pGW4BAI, in which each gene controlled by
several regulation elements for initiation and termination of
transcription and enhancement of translation. Leave stripes of *Nicotiana*
tabacum var. K326 were transformed with *Agrobacterium tumefaciens* strain
LBA4404 harboring the plant expression vector. PCR and Southern blotting
anal. showed the foreign *cryIA* and GNA gene being inserted into
the genome of transformed tobacco plants. Leaf disk bioassay against
cotton bollworm (*H. armigera*) showed transgenic tobacco plants having high
insecticidal activity. Inhibition of aphid population in leaf disk
bioassay against *Myzus persicae* showed fecundity of transgenic plants
being lower than that of on untransformed plants; the aphid population on
the transgenic tobacco plants being 25-70% of that of on untransformed
tobacco plant. Through the two bioassay against *H. armigera* and *M.*
persicae, several transgenic tobacco plants showing high insect resistant
activities to both pests were obtained.

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:800322 CAPLUS

DN 132:289336

TI Expression of two insect-resistant genes *cryIA* (b&c)/GNA in
transgenic tobacco plants results in added protection against both cotton
bollworm and aphids

AU Wang, Zhibin; Guo, Sandui

CS Laboratory of Biochemistry and Molecular Biology, Biotechnology Research
Center, Chinese Academy of Agricultural Sciences, Beijing, 100081, Peop.
Rep. China

SO Chinese Science Bulletin (1999), 44(22), 2051-2058

CODEN: CSBUEF; ISSN: 1001-6538

PB Science in China Press

DT Journal

LA English

AB The synthesized *Bacillus thuringiensis* insecticidal protein gene
cryIA (b&c) and the synthesized gene GNA, (the mannose specific
lectin from snowdrop (*Galanthus nivalis*)), *tumefaciens* have been

inserted into plant expression vector pGW4BAI. Leave stripes of *Nicotiana tabacum* var. K326 have been transformed with *Agrobacterium tumefaciens* strain LBA4404 harboring the plant expression vector. 28 Kanamycin resistant tobacco plants have been obtained. PCR and Southern blot analyses show that the foreign *cryIA* and *GNA* genes have been inserted into the genome of transformed tobacco plants. Hemagglutination assays show that *GNA* has a functional activity. Leaf disk bioassays against cotton bollworm (*H. armigera*) show that the transgenic tobacco plants have a high insecticidal activity. The inhibition of aphid population in leaf disk bioassays against *Myzus persicae* shows that the fecundity of aphid on transgenic plants is lower than that on untransformed plants; the aphid population on the transgenic tobacco plants is 25%-70% that on untransformed tobacco plants. ELISA anal. of *CryIA* protein in tobacco leaves provides similar data to bioassay results. Through the two bioassays against *H. armigera* and *M. persicae*, several transgenic tobacco plants showing high insect-resistant activities to both pests have been obtained.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:721555 CAPLUS
DN 132:47878
TI Partial purification and characterization of *Bacillus thuringiensis* CryIA toxin receptor A from *Heliothis virescens* and cloning of the corresponding cDNA
AU Oltean, Daniela I.; Pullikuth, Ashok K.; Lee, Hyun-Ku; Gill, Sarjeet S.
CS Environmental Toxicology and Graduate Programs and Department of Neuroscience, University of California, Riverside, CA, 92521, USA
SO Applied and Environmental Microbiology (1999), 65(11), 4760-4766
CODEN: AEMIDF; ISSN: 0099-2240
PB American Society for Microbiology
DT Journal
LA English
AB Although extensively studied, the mechanism of action of insecticidal *Bacillus thuringiensis* Cry toxins remains elusive and requires further elucidation. Toxin receptors in the brush border membrane demand particular attention as they presumably initiate the cascade of events leading to insect mortality after toxin activation. The 170-kDa CryIAC toxin-binding aminopeptidase from the tobacco budworm (*Heliothis virescens*) was partially purified, and its corresponding cDNA was cloned. The cDNA encodes a protein with a putative glycosyl phosphatidylinositol anchor and a polythreonine stretch clustered near the C terminus with predicted O-glycosylation. Partial purifn. of the 170-kDa aminopeptidase also resulted in isolation of a 130-kDa protein that was immunol. identical to the 170-kDa protein, and the two proteins had identical N termini. These proteins were glycosylated, as suggested by soybean agglutinin lectin blot results. CryIAC toxin affinity data for the two proteins indicated that the 130-kDa protein had a higher affinity than the 170-kDa protein. The data suggest that posttranslational modifications can have a significant effect on CryIAC toxin interactions with specific insect midgut proteins.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:307179 CAPLUS
DN 136:65624
TI Expression of multiple insecticidal genes confers broad resistance against a range of different rice pests
AU Maqbool, Shahina Bano; Riazuddin, Sheikh; Loc, Nguyen Thi; Gatehouse, Angharad M. R.; Gatehouse, John A.; Christou, Paul
CS Molecular Biotechnology Unit, John Innes Centre, Norwich, NR4 7UH, UK
SO Molecular Breeding (2001), 7(1), 85-93
CODEN: MOBRFL; ISSN: 1380-3743
PB Kluwer Academic Publishers
DT Journal
LA English
AB We report the simultaneous introduction of three insecticidal genes (the *Bt* genes *cryIAC* and *cry2A*, and the snowdrop lectin gene *gna*) into com. important indica rice varieties M7 and Basmati 370, by particle bombardment. Transgenic plants expressed *CryIAC*, *Cry2A* and *GNA* at different levels, either singly or in combination at 0.03-1%, 0.01-0.5% and 0.01-2.5% of total sol. protein, resp. The transgenes showed stable transmission and expression, and R1 transgenic plants provided significant ($p < 0.01$) protection against three of the most important insect pests of rice: rice leaf folder (*Cnaphalocrocis medinalis*), yellow stem borer (*Scirpophaga incertulas*) and brown planthopper (*Nilaparvata lugens*). The triple transformants showed significantly ($p < 0.05$) higher resistance to these insects than plants expressing single transgenes. Bioassays using the triple-transgenic plants showed 100% eradication of the rice leaf folder and yellow stem borer, and 25% redn. in the survival of the brown planthopper. The greatest redn. in insect survival, and the greatest redn. in plant damage, occurred in plants expressing all three transgenes. This approach maximises the utility of gene transfer technol. to introduce

combinations of genes whose products disrupt different biochem. or
physiol. processes in the same insect, providing a multi-mechanism
defense.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s ricin and cryi?
L4 1 RICIN AND CRYI?

=> d ti

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
TI Fusion proteins comprising *Bacillus thuringiensis* CryIA(b,c)
toxins and ricin B chain fragments and their pesticidal
activities

=> logoff hold
STN INTERNATIONAL SESSION SUSPENDED AT 13:32:06 ON 28 NOV 2003

FILE 'HOME' ENTERED AT 10:34:53 ON 12 DEC 2003

=> file agricola biosis caplus caba

=> s diphtheria and b and bind?
L1 480 DIPHTHERIA AND B AND BIND?

=> duplicate remove l1
L2 352 DUPLICATE REMOVE L1 (128 DUPLICATES REMOVED)

=> s l2 and review
L3 7 L2 AND REVIEW

=> d ti 1-7

L3 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Complete clinical resolution of peripheral T-cell lymphoma (Lennert's
variant) with denileukin diftotox (ONTAK(R)).

L3 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Involvement of small GTPases in the regulation of smooth muscle
contraction.

L3 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI ACTION AND PRODUCTION OF DIPHTHERIA TOXIN.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Translocation of diphtheria toxin across cellular membranes

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Protein engineering of DAB-IL-2 fusion toxins to increase biological
potency

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Transport of hydrophilic proteins across biological membranes: use of
diphtheria toxin as a model protein

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Biophysical properties of diphtheria toxin fragment B
in correlation to its binding ability to eukaryotic cell
membranes

=> d bib abs 4 6 7

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:655085 CAPLUS
DN 125:298250
TI Translocation of diphtheria toxin across cellular membranes
AU Olsnes, S.; Klingenberg, O.; Falnes, P. Oe.; Valdizan, E. M.; Lanzrein,
M.; Wiedlocha, A.
CS Institute Cancer Research, Norwegian Radium Hospital, Oslo, 0310, Norway
SO Zentralblatt fuer Bakteriologie, Supplement (1996), 28(Bacterial Protein
Toxins), 154-160
CODEN: ZBASE2; ISSN: 0941-018X
PB Fischer
DT Journal; General Review
LA English
AB A review with 18 refs. Transport of diphtheria toxin
to the cytosol is initiated by binding of the B
-fragment to specific cell surface receptors, the precursor of heparin
binding EGF-like growth factor. Translocation of the A-fragment
across cellular membranes is induced by low pH as obtained in endosomes
or, artificially, by acidification of the extracellular medium. In the

latter case, translocation occurs from the cell surface. Introduction of an artificial internal disulfide bond in the toxin A-fragment prevented translocation in both systems. When the artificial disulfide was located near the N-terminal end of the A-fragment, the protein became stuck in a partially translocated state. Also when the disulfide was located C-terminally the interfragment disulfide was reduced, but in this case the A-fragment was released into the medium. The intrafragment disulfide was not reduced in either case. The data indicate that translocation is initiated by transfer of the interfragment disulfide to the cytosol.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1992:17238 CAPLUS
 DN 116:17238
 TI Transport of hydrophilic proteins across biological membranes: use of diphtheria toxin as a model protein
 AU Madhus, I. H.; Moskaug, J. O.
 CS Inst. Cancer Res., Norw. Radium Hosp., Oslo, 0310, Norway
 SO Methodological Surveys in Biochemistry and Analysis (1991), 21(Cell Signalling: Exp. Strategies), 79-84
 CODEN: MSBADU; ISSN: 0748-6715
 DT Journal; General Review
 LA English
 AB A review, with 17 refs. Bacterial and plant toxins are the only examples of proteins known to enter the cytosol of eukaryotic cells when added in the medium. Diphtheria toxin (DT) has for several years been employed as a model protein in studies of protein translocation across biol. membranes. DT is synthesized as a single polypeptide chain by pathogenic strains of *Corynebacterium diphtheriae*, but the toxin is activated by proteolytic cleavage, yielding disulfide-linked fragments A and B. Entry can easily be assayed, because fragment A has ADP-ribosyl transferase activity, which inactivates elongation factor 2. Fragment B is responsible for receptor binding and membrane interaction. Both native DT and fragment B alone form cation-selective channels, measured as an influx of $^{22}\text{Na}^+$, when cells with surface-bound protein are exposed to low pH. The capacity for channel formation serves as a measure of whether the protein can be inserted properly into the membrane, and can be used in functional tests for DT mutants and DT-derived fusion proteins.

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1980:175217 CAPLUS
 DN 92:175217
 TI Biophysical properties of diphtheria toxin fragment B in correlation to its binding ability to eukaryotic cell membranes
 AU Lambotte, P.; Falmagne, P.; Capiiau, C.; Ruysschaert, J. M.; Dirx, J.
 CS Lab. Chim. Biol. Biophys., Univ. Etat Mons, Mons, Belg.
 SO Archives Internationales de Physiologie et de Biochimie (1979), 87(5), 1041-2
 CODEN: AIPBAY; ISSN: 0003-9799
 DT Journal; General Review
 LA English
 AB A review with 8 refs.

=> d bib abs 1-3, 5

L3 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:152389 BIOSIS
 DN PREV200200152389
 TI Complete clinical resolution of peripheral T-cell lymphoma (Lennert's variant) with denileukin diftotox (ONTAK(R)).
 AU Bernstein, Zale P. [Reprint author]; Miller, Kena [Reprint author]; Barcos, Maurice P.
 CS Oncology, Roswell Park Cancer Center, Buffalo, NY, USA
 SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 238b. print.
 Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 21 Feb 2002
 Last Updated on STN: 26 Feb 2002
 AB Peripheral T-cell lymphoma (PTCL), Lennert's variant, is known to follow a variable course and transform into an aggressive phase. The lymphoma cells tend to remain confined to lymph nodes; extranodal or cutaneous involvement is rare. Current therapies include doxorubicin-based combination chemotherapy. Patients generally respond poorly, relapse rate is high, and overall survival is poor. ONTAK (denileukin diftotox) is a cytotoxic fusion protein that contains the enzymatic and translocation domains of the diphtheria toxin, bound to human interleukin-2 (IL-2). ONTAK selectively binds to the IL-2 receptor and is internalized into the cell via endocytosis. Ultimately cell death occurs

as the diphtheria toxin enters the cytoplasm of the cell and acts to inhibit protein synthesis. Expression of the interleukin-2 receptor on the surface of various malignant cells of lymphoid origin forms the rationale for use of ONTAK in the T-cell non-Hodgkin lymphomas. ONTAK has been used for T-cell lymphomas that do not have cutaneous involvement, but data are very limited. LeMaistre, et al previously described a complete remission in one patient with diffuse large-cell immunoblastic (Lennert's) NHL (Blood, 91, 2, 1998). A 51-year-old male initially diagnosed with Hodgkin's disease had successful induction to remission with 6 cycles of ABVD. He was referred to our institution when his adenopathy recurred. At that time review of original pathology led to a revision of his initial diagnosis to that of PTCL, Lennert's variant. He then received one cycle of DHAC and progressed, and was given ICE but continued to progress. A thorough clinical and radiologic evaluation at that time showed rapid progression of disease with severe pruritus, increased lymphadenopathy, splenomegaly, malaise and fatigue. The patient then received eight 5-day courses of ONTAK given every 21 days. Doses increased from an initial 9mcg/kg to 21 mcg/kg/day. Over the course of ONTAK therapy, the patient showed improved appetite, weight stabilization, diminished fatigue, and resolution of rash and pruritus. Clinically the patient had complete resolution of his lymphadenopathy; however, the splenomegaly persisted. Adverse events included an episode of acute renal failure after the first cycle of ONTAK. Clinical response and chemical abnormalities suggested this may have been due to tumor lysis. Allopurinol and aggressive IV hydration were added to the drug regimen, and no further episodes of renal failure occurred. Other side effects were generally limited to the first 24 to 48 hours of each 5 day cycle. These included fevers, nausea and occasional hypotension (discontinuation of verapamil during course of ONTAK was effective in maintaining stable BP overall). Premedications included acetaminophen, dexamethasone, prochlorperazine, and aggressive IV hydration. As the patient's spleen appeared to have persistent disease, and he continued to have symptoms of splenomegaly (abdominal discomfort, early satiety), the patient elected to undergo splenectomy approximately 4 weeks after his eighth course of ONTAK. Pathological examination of his spleen suggested past but no definite present involvement by lymphoma. Flow cytometric analysis of this tissue revealed a high frequency of dead cells but without any evidence of T or B-cell malignancy. This experience suggests ONTAK may have some therapeutic benefit in non-cutaneous T-cell lymphomas.

L3 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:72681 BIOSIS
DN PREV199900072681
TI Involvement of small GTPases in the regulation of smooth muscle contraction.
AU Pfitzer, G. [Reprint author]; Arner, A.
CS Inst. Vegetative Physiologie, Univ. Koeln, Robert-Kochstr. 39, D-50931 Koeln, Germany
SO Acta Physiologica Scandinavica, (Dec., 1998) Vol. 164, No. 4, pp. 449-456. print.
CODEN: APSXAX. ISSN: 0001-6772.
DT Article
LA English
ED Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
AB Neurohumoral stimulation of smooth muscle leads to an increased responsiveness of the myofilaments to Ca^{2+} . This review provides a summary of the data that suggest that the signalling from the membrane-bound serpentine receptors to the contractile apparatus leading to the increase in Ca^{2+} -sensitivity requires the activation of the Ras-related low molecular mass GTPase Rho. In smooth muscle permeabilized with alpha-toxin or beta-escin, the increase in force elicited by different agonists at fixed (Ca^{2+}) (Ca^{2+} -sensitization) can be inhibited by bacterial toxins (EDIN, and exoenzyme C3) which ADP-ribosylate and inactivate Rho proteins. Moreover, the agonist-induced increase in Ca^{2+} -sensitivity can be mimicked by constitutively active recombinant Rho proteins. The physiological relevance of this mechanism is suggested by the fact that toxins that are internalized into intact cells (toxin B from *C. difficile* and a chimeric toxin (DC3B) consisting of C3 and the (non-catalytic) B fragment of diphtheria toxin (inhibit the tonic phase of an agonist-induced contraction. Toxin B inhibits contraction without affecting the intracellular Ca^{2+} -transient determined with fura-2. However, it inhibits phosphorylation of the regulatory light chains of myosin (MLC). Rho has been suggested to activate a Rho-associated kinase which in turn phosphorylates the myosin binding subunit of the myosin light chain phosphatase. This would lead to an increase in phosphorylation of MLC and hence of force at constant Ca^{2+} . The Ca^{2+} -sensitizing effect of agonists is also inhibited by tyrosine kinase inhibitors. This suggests the possibility that in smooth muscle, like in non-muscle cells, there is a cross-talk between Rho and tyrosine kinases.

L3 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1975:132072 BIOSIS
DN PREV197559032072; BA59:32072
TI ACTION AND PRODUCTION OF DIPHTHERIA TOXIN.
AU UCHIDA T
SO Japanese Journal of Bacteriology, (1974) Vol. 29, No. 4, pp. 651-664.
CODEN: NSKZAM. ISSN: 0021-4930.
DT Article
FS BA
LA Unavailable

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1993:99766 CAPLUS

DN 118:99766

TI Protein engineering of DAB-IL-2 fusion toxins to increase biological potency

AU Kiyokawa, Tetsuyuki; Williams, Diane P.; Snider, Catherine E.; Waters, Cory A.; Nichols, Jean C.; Strom, Terry B.; Murphy, John R.

CS Med. Cent., Boston Univ., Boston, MA, 02118, USA

SO Annals of the New York Academy of Sciences (1991), 636(Antigen Clone-Specific Immunoregul.), 331-9

CODEN: ANYAA9; ISSN: 0077-8923

DT Journal; General Review

LA English

AB A review, with 43 refs. The genetic replacement of either the native diphtheria toxin or Pseudomonas exotoxin A receptor binding domain with the eukaryotic cell receptor-specific polypeptide hormones or growth factor sequences has resulted in the development of a new class of biol. response modifier-the fusion toxin. The 1st of these fusion toxins, DAB486-interleukin-2 (IL-2), is currently in human phase I clin. trials and the early results clearly demonstrate that this mol. is safe, well-tolerated, and biol. active in the elimination of high-affinity IL-2 receptor-pos. leukemia and lymphoma cells without adverse side effect. DAB486-IL-2 is a bipartite fusion protein composed of diphtheria toxin fragment A and fragment B sequences to Ala486 linked to Pro2 through Thr133 of human IL-2. This chimeric protein is the product of a genetic fusion between a truncated gene encoding fragment A and the membrane-assocg. domains of fragment B of diphtheria toxin and a synthetic gene encoding human IL-2. DAB486-IL-2 has been shown to selectively bind to high-affinity IL-2 receptors, be internalized by receptor-mediated endocytosis, and facilitate the delivery of diphtheria toxin fragment A to the cytosol of target cells. Recent studies have defined the minimal size of fragment B that is required to deliver fragment A across the endocytic vesicle membrane in target cells, and defined the site of proteolytic processing involved in the release of fragment A from the intact fusion toxin mol.

=> s 12 and (carbohydrate or galact?)

L4 14962 12 AND (CHARBOHYDRATE OR GALACT?)

=>

=> s 12 and (carbohydrate or galact?)

L5 32129 12 AND (CARBOHYDRATE OR GALACT?)

=> s DIPHTHERIA AND B AND BIND? and (carbohydrate or galact?)

L6 25 DIPHTHERIA AND B AND BIND? AND (CARBOHYDRATE OR GALACT?)

=> d ti 1-25

L6 ANSWER 1 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

TI Efficient extracellular production of recombinant Escherichia coli heat-labile enterotoxin B subunit by using the expression/secretion system of Bacillus brevis and its mucosal immunoadjuvanticity.

L6 ANSWER 2 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

TI CLONING NUCLEOTIDE SEQUENCE AND HYBRIDIZATION STUDIES OF THE TYPE IIB HEAT-LABILE ENTEROTOXIN GENE OF ESCHERICHIA-COLI.

L6 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

TI IMMUNO TOXINS HYBRID MOLECULES OF MONO CLONAL ANTIBODIES AND A TOXIN SUBUNIT SPECIFICALLY KILL TUMOR CELLS.

L6 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

TI RICIN LINKED TO MONO PHOSPHO PENTA MANNOSE BINDS TO FIBROBLAST LYSOSOMAL HYDROLASE RECEPTORS RESULTING IN A CELL TYPE SPECIFIC TOXIN.

L6 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

TI Gene profiling methods of diagnosing potential for metastasis or developing hepatocellular carcinoma and of identifying therapeutic targets

L6 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

TI Gene expression profiles for diagnostic and prognostic grading of breast cancer and for drug screening

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Effects of iron limitation on adherence and cell surface carbohydrates of
 Corynebacterium diphtheriae strains

L6 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Methods for production of biochips and their use in cancer diagnosis and
 treatment

L6 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Modular biochip arrays and their diagnostic or analytical uses and their
 preparation and uses

L6 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Synthetic pre-trans-splicing molecules (PTM) encoding diphtheria toxin
 subunit A used for double RNA trans-splicing to disrupt human
 papillomavirus virus 16 genes for cervix carcinoma treatment

L6 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Endocrine disruptor screening using DNA chips of endocrine
 disruptor-responsive genes

L6 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Expression vector system and a method for optimization and confirmation of
 DNA delivery and quantification of targeting frequency

L6 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI A mammalian two-hybrid system for adenomatous polyposis coli-mutated colon
 cancer therapeutics

L6 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Albumin fusion proteins with therapeutic proteins for improved shelf-life

L6 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Glycoprotein antigens, antibodies specific thereto and method for
 producing same

L6 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Efficient extracellular production of recombinant Escherichia coli
 heat-labile enterotoxin B subunit by using the
 expression/secretion system of Bacillus brevis and its mucosal
 immunoadjuvanticity

L6 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Novel methods for therapeutic vaccination

L6 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Immunotoxins for preventing anti-Gal production in xenograft recipients

L6 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Immunoglobulin molecules having a synthetic variable region and modified
 specificity

L6 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Enhanced effects for hapten conjugated therapeutics

L6 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Targeted combination immunotherapy of cancer

L6 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Reaction columns for simultaneous multiple measurements and method for
 determination of compounds

L6 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Antibodies and autoantigen and methods for diagnosis and treatment of
 insulin-dependent diabetes mellitus

L6 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Covalently-linked complexes and methods for enhanced cytotoxicity and
 imaging

L6 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 TI Cloning, nucleotide sequence, and hybridization studies of the type IIb
 heat-labile enterotoxin gene of Escherichia coli

=> d bib abs 4 25

L6 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1980:184155 BIOSIS
 DN PREV198069059151; BA69:59151
 TI RICIN LINKED TO MONO PHOSPHO PENTA MANNOSE BINDS TO FIBROBLAST
 LYSOSOMAL HYDROLASE RECEPTORS RESULTING IN A CELL TYPE SPECIFIC TOXIN.
 AU YOUNG R J [Reprint author]; MURRAY G J; NEVILLE D M JR
 CS SECT BIOPHYS CHEM, LAB NEUROCHEM, NATL INST MENT HEALTH, BETHESDA, MD

20205, USA
 SO Proceedings of the National Academy of Sciences of the United States of America, (1979) Vol. 76, No. 11, pp. 5559-5562.
 CODEN: PNASA6. ISSN: 0027-8424.
 DT Article
 FS BA
 LA ENGLISH
 AB The receptor specificity of the plant seed toxin ricin, which ordinarily binds to galactose-containing receptors, was altered by coupling monophosphopentamannose residues to ricin by reductive amination and by reversibly binding lactose to the modified ricin. The added monophosphopentamannose residues provide ricin with the recognition factor common to fibroblast lysosomal hydrolases and enable the modified ricin (Man6P-ricin) to bind to the fibroblast Man6P receptor and inhibit protein synthesis in the cells via this receptor. The addition of lactose to Man6P-ricin saturates the galactose site on Man6P-ricin and prevents the binding of Man6P-ricin to cells via galactose-containing ricin receptors. The Man6P receptor-mediated toxicity of Man6P-ricin, identified in human fibroblasts by competition by Man6P and blockade by alkaline phosphatase treatment, was not detected in HeLa cells or human amnion cells. In the presence of lactose, the fibroblasts were 8 and 13 times more sensitive than amnion and HeLa cells, respectively. Highly toxic cell-type-specific reagents can be made by the proper alteration of toxin receptor specificities. An attempt to construct a highly toxic altered toxin by adding Man6P residues to diphtheria toxin fragment A was unsuccessful. A possible explanation is that in Man6P-ricin the ricin B chain performs some entry function, even though the initial binding step occurs at the Man6P receptor. The present work is a further attempt to construct a cell-type-specific cytotoxic reagent with potential antineoplastic activity utilizing the concepts previously developed for artificial hybrid proteins.

L6 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1990:173143 CAPLUS
 DN 112:173143
 TI Cloning, nucleotide sequence, and hybridization studies of the type IIb heat-labile enterotoxin gene of *Escherichia coli*
 AU Pickett, Carol L.; Twiddy, Edda M.; Coker, Christopher; Holmes, Randall K.
 CS Dep. Microbiol., Unif. Serv. Univ. Health Sci., Bethesda, MD, 20814, USA
 SO Journal of Bacteriology (1989), 171(9), 4945-52
 CODEN: JOBAAY; ISSN: 0021-9193
 DT Journal
 LA English
 AB Type IIb heat-labile enterotoxin (LT-IIb) is produced by *E. coli* 41. Restriction fragments of total cell DNA from strain 41 were cloned into a cosmid vector, and one cosmid clone that encoded LT-IIb was identified. The genes for LT-IIb were subcloned into a variety of plasmids, expressed in minicells, sequenced, and compared with the structural genes for other members of the *Vibrio cholerae*-*E. coli* enterotoxin family. The A subunits of these toxins all have similar ADP-ribosyltransferase activity. The A genes of LT-IIa and LT-IIb exhibited 71% DNA sequence homol. with each other and 55 to 57% homol. with the A genes of cholera toxin (CT) and the type I enterotoxins of *E. coli* (LTh-I and LTp-I). The A subunits of the heat-labile enterotoxins also have limited homol. with other ADP-ribosylating toxins, including pertussis toxin, diphtheria toxin, and *Pseudomonas aeruginosa* exotoxin A. The B subunits of LT-IIa and LT-IIb differ from each other and from type I enterotoxins in their carbohydrate-binding specificities. The B genes of LT-IIa and LT-IIb were 66% homologous, but neither had significant homol. with the B genes of CT, LTh-I, and LTp-I. The A subunit genes for the type I and type II enterotoxins represent distinct branches of an evolutionary tree, and the divergence between the A subunit genes of LT-IIa and LT-IIb is greater than that between CT and LT-I. In contrast, it has not yet been possible to demonstrate an evolutionary relationship between the B subunits of type I and type II heat-labile enterotoxins. Hybridization studies with DNA from independently isolated LT-II producing strains of *E. coli* also suggested that addnl. variants of LT-II exist.

=> d bib abs 7

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2003:835989 CAPLUS
 TI Effects of iron limitation on adherence and cell surface carbohydrates of *Corynebacterium diphtheriae* strains
 AU Moreira, Lilian de Oliveira; Andrade, Arnaldo Feitosa Braga; Andrade, Braga; Vale, Marcio Damasceno; Souza, Sonia Maria Silva; Hirata, Raphael, Jr.; Asad, Lidia Maria Oliveira Buarque; Asad, Nasser Ribeiro; Monteiro-Leal, Luiz Henrique; Previato, Jose Osvaldo; Mattos-Guaraldi, Ana Luiza
 CS Faculdade de Ciencias Medicas, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil
 SO Applied and Environmental Microbiology (2003), 69(10), 5907-5913

PB CODEN: AEMIDF; ISSN: 0099-2240
DT American Society for Microbiology
LA Journal
AB English

AB Iron limitation may cause bacterial pathogens to grow more slowly; however, it may also stimulate these microorganisms to produce greater tissue damage, given that many virulence factors are controlled by the iron supply in the environment. The present study investigated the influence of low iron availability on the expression of proteins and surface sugar residues of two toxigenic strains of *Corynebacterium diphtheriae* subsp. *mitis* and evaluated their adherence to human group B erythrocytes and HEp-2 cells. A comparison was made between bacteria grown in (i) Trypticase soy broth (TSB), (ii) TSB treated with dipyrldyl to deplete free iron, and (iii) TSB enriched with FeCl₃. The effects of iron concn. on adhesive properties were different for strains 241 and CDC-E8392, of the sucrose-fermenting and non-sucrose-fermenting biotypes, resp. Iron-limited conditions enhanced interaction of strain 241 with erythrocytes and HEp-2 cells. Inhibition assays suggested the involvement of nonfimbrial protein combination 67-72p on hemagglutination of *diphtheria* bacilli grown under iron-limited conditions. Conversely, iron limitation inhibited adherence to glass and expression of electron-dense material on the bacterial surface. Lectin binding assays demonstrated a redn. in the no. of sialic acid residues and an increase in D-mannose and D-galactose residues on the surfaces of both strains. Thus, iron exerts a regulatory role on adhesive properties of *diphtheria* bacilli, and low iron availability modulates the expression of *C. diphtheriae* surface carbohydrate moieties. The significant changes in the degree of lectin binding specific for D-mannose, D-galactose and sialic acid residues may have an effect on binding of host cells. The expression of dissimilar microbial virulence determinants may be coordinately controlled by common regulatory systems. For *C. diphtheriae*, the present results imply regulation of adherence and slime prodn. as part of a global response to iron-limited environmental conditions that includes derepression of genes for the synthesis of cytotoxin and siderophores and for transport of the Fe(III)-siderophore complexes.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs 17

L6 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:240985 CAPLUS
DN 132:292701
TI Novel methods for therapeutic vaccination
IN Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla
PA M & E Biotech A/S, Den.
SO PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020027	A2	20000413	WO 1999-DK525	19991005
	WO 2000020027	A3	20001012		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2345817	AA	20000413	CA 1999-2345817	19991005
	AU 9958510	A1	20000426	AU 1999-58510	19991005
	AU 751709	B2	20020822		
	EP 1117421	A2	20010725	EP 1999-945967	19991005
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO			
	JP 2002526419	T2	20020820	JP 2000-573386	19991005
	EE 200100203	A	20021015	EE 2001-203	19991005
	NO 2001001586	A	20010531	NO 2001-1586	20010328
	ZA 2001002603	A	20020930	ZA 2001-2603	20010329
	HR 2001000319	A1	20020630	HR 2001-319	20010504
PRAI	DK 1998-1261	A	19981005		
	US 1998-105011P	P	19981020		
	WO 1999-DK525	W	19991005		

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably

self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

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